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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,259	02/20/2004	Kenichiro Hasumi	358690-00005-1	7322
<div>7590 Debra Z. Anderson Eckert Seamans Cherin & Mellott, LLC 44th Floor 600 Grant Street Pittsburgh, PA 15219</div>			<div>EXAMINER HUMPHREY, LOUISE WANG ZHIYING</div>	
			<div>ART UNIT 1648</div>	
			<div>MAIL DATE 07/10/2009</div>	
			<div>DELIVERY MODE PAPER</div>	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/783,259

Applicant(s)

HASUMI ET AL.

Examiner

LOUISE HUMPHREY

Art Unit

1648

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 June 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-16 is/are pending in the application.
- 4a) Of the above claim(s) 3-5, 7, 8 and 12-15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 6, 9-11 and 16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03 June 2009 has been entered.

DETAILED ACTION

This Office Action is in response to the amendment filed 03 June 2009. Claim 2 has been cancelled. Claim 16 is added. Claims 1 and 3-16 are pending. Claims 3-5, 7, 8 and 12-15 are withdrawn. Claims 1, 6, 9-11, and 16 are currently examined.

Affidavit or Declaration under 37 CFR 1.132

The declaration/affidavit by Dr. Dean Mann under 37 CFR 1.132 filed on 03 June 2009 is sufficient to overcome the rejection of claims 1, 6 and 9-11 based upon the Kato and Mengozzi references and Setaluri patent as set forth in the last Office action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

WITHDRAWN REJECTIONS

The rejection of claim 1 under 35 U.S.C. §103(a) as being obvious over Kato *et al.* (2001, IDS 15 October 2007) in view of Mengozzi *et al.* (2001) **is withdrawn** in response to Applicants' amendment.

The rejection of claim 6 under 35 U.S.C. §103(a) as being obvious over Kato *et al.* (2001, IDS 15 October 2007) in view of Mengozzi *et al.* (2001) and Meidenbauer *et al.* (2000) **is withdrawn** in response to Applicants' amendment.

The rejection of claims 9-11 under 35 U.S.C. §103(a) as being obvious over Kato *et al.* (2001, IDS 15 October 2007) in view of Mengozzi *et al.* (2001) and Setaluri *et al.* (US 2002/0192727) **is withdrawn** in response to Applicants' amendment.

Response to Arguments

Applicant's arguments with respect to claims 1, 6 and 9-11 have been considered but are moot in view of the following new ground of rejection.

NEW REJECTIONS

Claims 1, 6, 9-11 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meidenbauer *et al.* (2000) in view of Baxevanis *et al.* (1997) and Quinn *et al.* (1998).

The instant invention is directed to a method comprising administering to a mammal an antigen, specifically a prostate-specific antigen (PSA), in combination with

the supernatant of lymphocyte conditioned medium, derived from peripheral blood mononuclear cells activated with anti-CD3 and anti-CD28-coated beads in a culture medium.

Meidenbauer *et al.* discloses administering a vaccine comprising PSA in combination with an adjuvant (Abstract; page 89, 2nd column, to page 90). The injection is done monthly subcutaneously with 125 µg adjuvant (page 90, right column, Vaccination Schema).

Meidenbauer *et al.* does not disclose the supernatant of lymphocyte conditioned medium, derived from peripheral blood mononuclear cells activated with anti-CD3 and anti-CD28-coated beads in a culture medium.

Baxevanis *et al.* discloses administering to patients cytokine-rich supernatants derived from cultures of peripheral blood mononuclear cells (PBMC) from healthy donors stimulated with anti-CD3 monoclonal antibodies (MAb) (page 1072-1073, see the paragraph connecting the two pages) coated on flasks (page 1075, left column, third paragraph). Anti-CD3-stimulated PBMC secrete high levels of IL-1 β , IL-2, IL-6, IL-7, IL-12 and GM-CSF, TNF- α and IFN- γ . These cytokines are potent inducers of anti-tumor cytotoxicity by activating both effectors with specificity against autologous tumors and effectors that lyse a broad spectrum of allogeneic tumors (page 1079, left column, second complete paragraph).

Neither Meidenbauer *et al.* nor Baxevanis *et al.* discloses the anti-CD28 antibody co-immobilized with anti-CD3 antibody on the beads in the PBMC culture medium for the preparation of cytokine-rich supernatants.

Quinn *et al.* discloses co-stimulation of PBMC with beads coated with co-immobilized anti-CD3 and anti-CD28 MAbs (page 1458, right column, last paragraph). Costimulation induces cytokines more effectively when both signals are provided together *in cis*, which is considered more realistic of interactions between a T cell and an antigen presenting cell (page 1458, left column, first complete paragraph). By cross-linking the CD3 and CD28 receptors with the anti-CD3-anti-CD28-coimmobilized beads, these MAbs mimic *in vivo* signaling events, leading to augmented endogenous cytokine production. See Abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the antigen-adjuvant combination of Meidenbauer *et al.* by adding the supernatant of stimulated PBMC culture, as taught by Baxevanis *et al.* The skilled artisan would have been motivated to do so to improve the immunogenic property of the administered antigen. Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the T cell activation procedure of Baxevanie *et al.* by replacing the anti-CD3-coated plates with anti-CD3 and anti-CD28-coated beads for co-stimulation of PBMC, as taught by Quinn *et al.* The skilled artisan would have been motivated to do so to more effectively induce cytokine secretion so that the supernatants would contain more cytokines that facilitate cytotoxic immune response to the administered antigen. Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./
Examiner, Art Unit 1648

/Jeffrey S. Parkin/
Primary Examiner, Art Unit 1648

1 July 2009